Claims

What is claimed is:

1. A formulation for the treatment of fungus-induced rhinosinusitis in a mammal, said formulation comprising:

(a) about 1 to about 700 mcg of a steroidal anti-inflammatory, wherein the steroidal anti-inflammatory is fluticasone or a pharmaceutically acceptable derivative thereof, said steroidal anti-inflammatory having the following particle size distribution profile:

i. about 10% of the steroidal anti-inflammatory particles have a particle size of less than 0.90 microns;

ii. about 25% of the steroidal anti-inflammatory particles have a particle size of less than 1.6 microns;

iii. about 50% of the steroidal anti-inflammatory particles have a particle size of less than 3.2 microns;

iv. about 75% of the steroidal anti-inflammatory particles have a particle size of less than 6.2 microns; and

v. about 90% of the steroidal anti-inflammatory particles have a particle size of less than 10.0 microns;

wherein said formulation is suitable for administration to the nasal-paranasal mucosa.

2. A formulation for the treatment of fungus-induced rhinosinusitis in a mammal, said formulation comprising:

(a) about 1 to about 700 mcg a steroidal anti-inflammatory, wherein the steroidal anti-inflammatory is beclomethasone or a pharmaceutically acceptable derivative thereof, said steroidal anti-inflammatory having the following particle size distribution profile:

i. about 10% of the steroidal anti-inflammatory particles have a particle size of less than 0.75 microns;

ii. about 25% of the steroidal anti-inflammatory particles have a particle size of less than 1.5 microns;

iii. about 50% of the steroidal anti-inflammatory particles have a particle size of less than 2.0 microns;

iv. about 75% of the steroidal anti-inflammatory particles have a particle size of less than 3.5 microns; and

v. about 90% of the steroidal anti-inflammatory particles have a particle size of less than 5.0 microns.

wherein said formulation is suitable for administration to the nasal-paranasal mucosa.

3. The formulation of claims 1 or 2, further comprising about 0.5 to about 150 mg of an antifungal agent..

4. The formulation of claim 3, wherein the antifungal agent is amphotericin β.

5. The formulation of claim 3, wherein said formulation comprises about 7.5 to about 15 mg of amphotericin β.

6. The formulation of claim 3, wherein said formulation comprises about 10 mg of amphotericin β.

7. The formulation of claim 3, wherein said formulation comprises about 20 to about 70 mg of fluconazole or itraconazole.

8. The formulation of claim 3, wherein said formulation comprises about 25 to about 50 mg of fluconazole or itraconazole.

9. The formulation of claim 3, wherein said formulation comprises about 30 mg of fluconazole or itraconazole.

10. The formulation of claim 1, comprising about 25 to about 400 mcg of said steroidal anti-inflammatory.

11. The formulation of claim 1, comprising about 75 to about 300 mcg of said steroidal anti-inflammatory.

12. The formulation of claim 1, comprising about 200 mcg of said steroidal anti-inflammatory.

13. The formulation of claim 10, wherein the steroidal anti-inflammatory has the following particle size distribution profile:

i. about 10% or less of the steroidal anti-inflammatory particles have a particle size of less than 0.90 microns;

ii. about 25% or less of the steroidal anti-inflammatory particles have a particle size of less than 1.6 microns;

iii. about 50% or less of the steroidal anti-inflammatory particles have a particle size of less than 3.2 microns;

iv. about 75% or less of the steroidal anti-inflammatory particles have a particle size of less than 6.10 microns; and,

v. about 90% or less of the steroidal anti-inflammatory particles have a particle size of less than 10 microns.

14. The formulation of claim 1, wherein the steroidal anti-inflammatory is fluticasone propionate having the following particle size distribution profile:

i. about 10% of the steroidal anti-inflammatory particles have a particle size of less than 0.70 microns;

ii. about 25% of the steroidal anti-inflammatory particles have a particle size of less than 1.30 microns;

iii. about 50% of the steroidal anti-inflammatory particles have a particle size of less than 2.5 microns;

iv. about 75% of the steroidal anti-inflammatory particles have a particle size of less than 4.0 microns;

v. about 90% of the steroid particles have a particle size of less than 6.0 microns; and,

vi. greater than 90% or about 100% of the steroidal anti-inflammatory particles have a particle size of less than 10 microns.

15. The formulation of claim 1, wherein the steroidal anti-inflammatory is fluticasone propionate having the following particle size distribution profile:

i. about 10% of the steroidal anti-inflammatory particles have a particle size less than 0.50 microns;

ii. about 25% of the steroidal anti-inflammatory particles have a particle size less than 0.90 microns;

iii. about 50% of the steroidal anti-inflammatory particles have a particle size less than 1.7 microns;

iv. about 75% of the steroidal anti-inflammatory particles have a particle size less than 3.5 microns; and,

v. about 90% of the steroidal anti-inflammatory particles have a particle size less than 5.5 microns.

16. The formulation of claim 2, comprising about 0.2 to about 3 mg of said steroidal anti-inflammatory.

17. The formulation of claim 2, comprising about 0.2 to about 2 mg of said steroidal anti-inflammatory.

18. The formulation of claim 2, comprising about 0.8 mg of said steroidal anti-inflammatory.

19. The formulation of claim 16, wherein the steroidal anti-inflammatory has the following particle size distribution profile:

i. about 10% of the steroidal anti-inflammatory particles have a particle size of less than 0.35 microns;

ii. about 25% of the steroidal anti-inflammatory particles have a particle size of less than 0.70 microns;

iii. about 50% of the steroidal anti-inflammatory particles have a particle size of less than 1.25 microns;

iv. about 75% of the steroidal anti-inflammatory particles have a particle size of less than 2.0 microns;

v. about 90% of the steroidal anti-inflammatory particles have a particle size of less than 3.0 microns; and,

vi. greater than 90% or about 100% of the steroidal anti-inflammatory particles have a particle size of less than 6.5 microns.

20. The formulation of claim 16, wherein the steroidal anti-inflammatory has the following particle size distribution profile:

i. about 10% of the steroidal anti-inflammatory particles have a particle size less than 0.40 microns;

ii. about 25% of the steroidal anti-inflammatory particles have a particle size less than 0.70 microns;

iii. about 50% of the steroidal anti-inflammatory particles have a particle size less than 1.3 microns;

iv. about 75% of the steroidal anti-inflammatory particles have a particle size less than 2.0 microns;

v. about 90% of the steroidal anti-inflammatory particles have a particle size less than 3.0 microns; and,

vi. greater than 90% or about 100% of the steroidal anti-inflammatory particles have a particle size less than 6.0 microns.

21. The formulation of claim 16, wherein the steroidal anti-inflammatory is beclomethasone dipropionate having the following particle size distribution profile:

i. about 10% of the steroidal anti-inflammatory particles have a particle size less than 0.60 microns;

ii. 25% of the steroidal anti-inflammatory particles have a particle size less than 0.90 microns;

iii. about 50% of the steroidal anti-inflammatory particles have a particle size less than 1.5 microns;

iv. about 75% of the steroidal anti-inflammatory particles have a particle size less than 2.5 microns;

v. about 90% of the steroidal anti-inflammatory particles have a particle size less than 3.5 microns; and,

vi. greater than 90% or about 100% of the steroidal anti-inflammatory particles have a particle size less than 6.0 microns.

22. The formulation of claim 1, wherein the formulation is sterile.

23. The formulation of claim 1, wherein the formulation further comprises a preservative.

24. The formulation of claim 23, wherein the preservative is benzalkonium chloride.

25. The formulation of claim 1, wherein the formulation is stable.

26. The formulation of claim 1, wherein the formulation is an aqueous suspension or aqueous solution.

27. The formulation of claim 26, wherein the formulation is in a metered-dose spray pump bottle.

28. The formulation of claim 26, further comprising about 0.01% to about 90% by weight on a dried weight basis of one or more of the following compounds:

(a) microcrystalline cellulose;

(b) carboxymethyl cellulose sodium;

(c) dextrose;

(d) benzalkonium chloride;

(e) polysorbate 80; and

(g) phenylethyl alcohol.

29. The formulation of claim 1, further comprising an antibiotic.

30. The formulation of claim 29, wherein the antibiotic is one or more selected from the group consisting of Amikacin, Azithromycin, Aztreonan, Cefazolin, Cefepine, Cefonicid, Cefaperazone, Cefotaxime, Cefotetan, Cefoxitin, Ceftazidime, Ceftizoxime, Ceftriaxone, Cefuroxime, Cephapirin, Ciprofloxacin, Clindamycin, Doxycycline, Erythromycin Lactobionate, Gentamicin, Kanamycin, Linezolid, Mezlocillin, Mupirocin, Nafcillin, Netilmicin, Neomycin, Oxacillin, Paromomycin, Piperacillin, Streptomycin, Ticarcillin, Tobramycin, and Vancomycin.

31. The formulation of claim 29, wherein the formulation comprises about 1 to about 800 mg of neomycin sulfate.

32. The formulation of claim 29, wherein the formulation comprises about 5 to about 500 mg of neomycin sulfate.

33. The formulation of claim 29, wherein the formulation comprises about 50 to about 300 mg of neomycin sulfate.

34. The formulation of claim 29, wherein the formulation comprises about 150 mg of neomycin sulfate.

35. A formulation for the treatment of fungus-induced rhinosinusitis, said formulation comprising:

(a) about 7.5 to about 15 mg of amphotericin β;

(b) about 75 to about 300 mcg of the steroidal anti-inflammatory fluticasone propionate having the following particle size distribution profile:

ii. about 10% of the steroidal anti-inflammatory particles have a particle size of less than 0.70 microns;

iii. about 25% of the steroidal anti-inflammatory particles have a particle size of less than 1.30 microns;

iv. about 50% of the steroidal anti-inflammatory particles have a particle size of less than 2.5 microns;

v. about 75% of the steroidal anti-inflammatory particles have a particle size of less than 4.0 microns;

vi. about 90% of the steroid particles have a particle size of less than 6.0 microns; and,

vii. greater than 90% or about 100% of the steroidal anti-inflammatory particles have a particle size of less than 10 microns.

wherein said formulation is suitable for administration to the nasal-paranasal mucosa.

36. A formulation for the treatment of fungus-induced rhinosinusitis, said formulation comprising:

(a) about 7.5 to about 15 mg of amphotericin β;

(b) about 0.2 to about 2 mg of the steroidal anti-inflammatory beclomethasone dipropionate having the following particle size distribution range;

ii. about 10% of the steroidal anti-inflammatory particles have a particle size less than 0.40 microns

iii. about 25% of the steroidal anti-inflammatory particles have a particle size less than 0.70 microns;

iv. about 50% of the steroidal anti-inflammatory particles have a particle size less than 1.3 microns;

v. about 75% of the steroidal anti-inflammatory particles have a particle size less than 2.0 microns;

vi. about 90% of the steroidal anti-inflammatory particles have a particle size less than 3.0 microns; and,

vii. greater than 90% or about 100% of the steroidal anti-inflammatory particles have a particle size less than 6.0 microns;

wherein said formulation is suitable for administration to the nasal-paranasal mucosa.

37. The formulation of claim 35 or 36, further comprising about 50 to about 250 mg of the antibiotic neomycin sulfate.

38. The formulation of claim 37, wherein said formulation is a sterile aqueous solution or aqueous suspension suitable for administration to the nasal-paranasal mucosa via a metered-dose spray pump bottle.

39. The formulation of claim 38, further comprising about 0.01% to about 90% by weight on a dried weight basis of one or more of the following compounds:

(a) microcrystalline cellulose;

(b) carboxymethyl cellulose sodium;

(c) dextrose;

(d) benzalkonium chloride;

(e) polysarbate 80; and

(g) phenylethyl alcohol.

40. A formulation for the treatment of fungus-induced rhinosinusitis, said formulation comprising:

(a) about 25 to about 45 mg of fluconazole or itraconazole;

(b) about 75 to about 300 mcg of the steroidal anti-inflammatory fluticasone propionate having the following particle size distribution profile:

ii. about 10% of the steroidal anti-inflammatory particles have a particle size of less than 0.70 microns;

iii. about 25% of the steroidal anti-inflammatory particles have a particle size of less than 1.30 microns;

iv. about 50% of the steroidal anti-inflammatory particles have a particle size of less than 2.5 microns;

v. about 75% of the steroidal anti-inflammatory particles have a particle size of less than 4.0 microns;

vi. about 90% of the steroid particles have a particle size of less than 6.0 microns; and,

vii. greater than 90% or about 100% of the steroidal anti-inflammatory particles have a particle size of less than 10 microns.

wherein said formulation is suitable for administration to the nasal-paranasal mucosa.

41. A formulation for the treatment of fungus-induced rhinosinusitis, said formulation comprising:

(a) about 25 to about 45 mg of fluconazole or itraconazole;

(b) about 0.2 to about 2 mg of the steroidal anti-inflammatory beclomethasone dipropionate having the following particle size distribution range;

ii. about 10% of the steroidal anti-inflammatory particles have a particle size less than 0.40 microns

iii. about 25% of the steroidal anti-inflammatory particles have a particle size less than 0.70 microns;

iv. about 50% of the steroidal anti-inflammatory particles have a particle size less than 1.3 microns;

v. about 75% of the steroidal anti-inflammatory particles have a particle size less than 2.0 microns;

vi. about 90% of the steroidal anti-inflammatory particles have a particle size less than 3.0 microns; and,

vii. greater than 90% or about 100% of the steroidal anti-inflammatory particles have a particle size less than 6.0 microns;

wherein said formulation is suitable for administration to the nasal-paranasal mucosa.

42. The formulation of claim 40 or 41, further comprising about 50 to about 250 mg of the antibiotic neomycin sulfate.

43. The formulation of claim 42, wherein said formulation is a sterile aqueous solution or aqueous suspension suitable for administration to the nasal-paranasal mucosa via a metered-dose spray pump bottle.

44. The formulation of claim 43, further comprising about 0.01% to about 90% by weight on a dried weight basis of one or more of the following compounds:

(a) microcrystalline cellulose;

(b) carboxymethyl cellulose sodium;

(c) dextrose;

(d) benzalkonium chloride;

(e) polysarbate 80; and

(g) phenylethyl alcohol.

45. A method of treating fungus-induced rhinosinusitis in a mammal, said method comprising the steps of applying to the mammal's nasal-paranasal mucosa a formulation comprising:

(a) about 1 to about 700 mcg of a steroidal anti-inflammatory, wherein the steroidal anti-inflammatory is fluticasone or a pharmaceutically acceptable derivative thereof, said steroidal anti-inflammatory having the following particle size distribution profile:

i. about 10% of the steroidal anti-inflammatory particles have a particle size of less than 0.90 microns;

ii. about 25% of the steroidal anti-inflammatory particles have a particle size of less than 1.6 microns;

iii. about 50% of the steroidal anti-inflammatory particles have a particle size of less than 3.2 microns;

iv. about 75% of the steroidal anti-inflammatory particles have a particle size of less than 6.2 microns; and

v. about 90% of the steroidal anti-inflammatory particles have a particle size of less than 10.0 microns.

46. A method of treating fungus-induced rhinosinusitis in a mammal, said method comprising the steps of applying to the mammal's nasal-paranasal mucosa a formulation comprising:

(a) about 1 to about 700 mcg a steroidal anti-inflammatory, wherein the steroidal anti-inflammatory is beclomethasone or a pharmaceutically acceptable derivative thereof, said steroidal anti-inflammatory having the following particle size distribution profile:

i. about 10% of the steroidal anti-inflammatory particles have a particle size of less than 0.75 microns;

ii. about 25% of the steroidal anti-inflammatory particles have a particle size of less than 1.5 microns;

iii. about 50% of the steroidal anti-inflammatory particles have a particle size of less than 2.0 microns;

iv. about 75% of the steroidal anti-inflammatory particles have a particle size of less than 3.5 microns; and

v. about 90% of the steroidal anti-inflammatory particles have a particle size of less than 5.0 microns.

wherein said formulation is suitable for administration to the nasal-paranasal mucosa.

47. The method of claims 45 or 46, further comprising the step of treating the mammal with an antifungal agent selected from the group consisting of amphotericin β, fluconazole, and itraconazole.

48. The method of claim 47, wherein said formulation comprises about 4 mg to about 30 mg of amphotericin β.

49. The method of claim 47, wherein said formulation comprises about 10 mg of amphotericin β.

50. The method of claim 47, wherein said formulation comprises about 20 to about 70 mg of fluconazole or itraconazole.

51. The method of claim 47, wherein said formulation comprises about 30 mg of fluconazole or itraconazole.

52. The method of claim 45, wherein said formulation comprises about 25 to about 400 mcg of said steroidal anti-inflammatory.

53. The method of claim 52, wherein the steroidal anti-inflammatory has the following particle size distribution profile:

i. about 10% or less of the steroidal anti-inflammatory particles have a particle size of less than 0.90 microns;

ii. about 25% or less of the steroidal anti-inflammatory particles have a particle size of less than 1.6 microns;

iii. about 50% or less of the steroidal anti-inflammatory particles have a particle size of less than 3.2 microns;

iv. about 75% or less of the steroidal anti-inflammatory particles have a particle size of less than 6.10 microns; and,

v. about 90% or less of the steroidal anti-inflammatory particles have a particle size of less than 10 microns.

54. The method of claim 52, wherein the steroidal anti-inflammatory is fluticasone propionate having the following particle size distribution profile:

i. about 10% of the steroidal anti-inflammatory particles have a particle size less than 0.50 microns;

ii. about 25% of the steroidal anti-inflammatory particles have a particle size less than 0.90 microns;

iii. about 50% of the steroidal anti-inflammatory particles have a particle size less than 1.7 microns;

iv. about 75% of the steroidal anti-inflammatory particles have a particle size less than 3.5 microns; and,

v. about 90% of the steroidal anti-inflammatory particles have a particle size less than 5.5 microns.

55. The method of claim 46, wherein said formulation comprises about 0.2 to about 3 mg of said steroidal anti-inflammatory.

56. The method of claim 46, wherein said formulation comprises about 0.8 mg of said steroidal anti-inflammatory.

57. The method of claim 55, wherein the steroidal anti-inflammatory has the following particle size distribution profile:

i. about 10% of the steroidal anti-inflammatory particles have a particle size of less than 0.35 microns;

ii. about 25% of the steroidal anti-inflammatory particles have a particle size of less than 0.70 microns;

iii. about 50% of the steroidal anti-inflammatory particles have a particle size of less than 1.25 microns;

iv. about 75% of the steroidal anti-inflammatory particles have a particle size of less than 2.0 microns;

v. about 90% of the steroidal anti-inflammatory particles have a particle size of less than 3.0 microns; and,

vi. greater than 90% or about 100% of the steroidal anti-inflammatory particles have a particle size of less than 6.5 microns.

58. The method of claim 55, wherein the steroidal anti-inflammatory is beclomethasone dipropionate having the following particle size distribution profile:

i. about 10% of the steroidal anti-inflammatory particles have a particle size less than 0.60 microns;

ii. 25% of the steroidal anti-inflammatory particles have a particle size less than 0.90 microns;

iii. about 50% of the steroidal anti-inflammatory particles have a particle size less than 1.5 microns;

iv. about 75% of the steroidal anti-inflammatory particles have a particle size less than 2.5 microns;

v. about 90% of the steroidal anti-inflammatory particles have a particle size less than 3.5 microns; and,

vi. greater than 90% or about 100% of the steroidal anti-inflammatory particles have a particle size less than 6.0 microns.

59. The method of claim 45 or 46, wherein the formulation is a sterile aqueous suspension or aqueous solution.

60. The method of claim 59, wherein the formulation is in a metered-dose spray pump bottle.

61. The method of claim 60, wherein the formulation is administered to said mammal as one spray in each nostril from 1 to about 10 times per day.

62. The method of claim 45 or 46wherein said formulation is administered topically to the nasal-paranasal mucosa of said mammal from 1 to about 10 times per day.

63. The method of claim 45 or 46, further comprising the step of administering an antibiotic to said mammal, wherein said mammal is diagnosed with a bacterial infection of the nasal-paranasal mucosa.

64. The method of claim 63, wherein the antibiotic is administered orally.

65. The method of claim 63, wherein the antibiotic is administered intranasally.

66. The method of claim 65, wherein the antibiotic is neomycin sulfate.

67. The method of claim 45 or 46, wherein said formulation further comprises an antibiotic.

68. The method of claim 67, wherein the formulation comprises about 1 to about 800 mg of neomycin sulfate.

69. The formulation of claim 67, wherein the formulation comprises about 50 to about 300 mg of neomycin sulfate.

70. The method of claim 67, wherein the formulation is a sterile aqueous suspension or aqueous solution in a metered-dose spray pump bottle, and wherein the formulation is administered to said mammal as one spray in each nostril from 1 to about 10 times per day.